D_1 receptor 3 or complement receptor 4 effective in downregulating production of interleukin-12, thereby treating the inflammatory bowel disease.

D_2 10. (Amended) The method of claim 7 or 8, wherein the ligand of complement receptor 3 is selected from the group consisting of iC3b, ICAM-1, fibrinogen, β-glucan, C3b, ICAM-2, ICAM-3, a complement receptor 3-binding microorganism, a complement receptor 3-binding product of a complement receptor 3-binding microorganism and antibodies to complement receptor 3.

Please cancel claims 1-6 without prejudice.

REMARKS

Claims 1-8 and 10 are pending in the present application. Claims 1-6 are canceled herein without prejudice. Claims 7 and 10 are amended herein for clarity and to more particularly define the invention. Support for these amendments can be found throughout the specification as well as in claims 7 and 10, as filed. No new matter is believed to be added by these amendments. In light of these amendments and the following remarks, applicants respectfully request reconsideration of this application and allowance of the pending claims to issue.

Applicants appreciate the opportunity to telephonically interview this case on January 30, 2003 with Examiners DeCloux and Nolan. The following remarks more specifically address the issues discussed in the interview.

Rejections Under 35 U.S.C. § 102(b)

A. The Office Actions states that claims 1-8 and 10 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Rosen et al. (WO 89/04174, published May 18, 1989). Further stated in the Office Action is that Rosen et al. teaches a method of administering an antibody with specificity for CR3 for the treatment or prophylaxis of inflammatory autoimmune and hypersensitivity diseases, and in particular inflammatory bowel disease, and consequently its symptoms, as recited in the instant claims. The Office Action goes on to state that although the referenced teachings do not explicitly teach that administration of antibodies directed to CR3 downregulates interleukin-12 in a subject or treats an interleukin-12 induced inflammatory response, down regulation of interleukin-12 in a subject and treatment of an interleukin-12-induced inflammatory response would be inherent properties effected by administration of antibodies against CR3. Therefore, according to the Office Action, the referenced teachings anticipate the claimed invention.

Claims 1-6 are canceled herein. As amended herein, claim 7 recites a method of treating inflammatory bowel disease in a human subject, comprising administering to a subject an amount of a ligand of complement receptor 3 or complement receptor 4 effective in downregulating interleukin-12 production, thereby treating the inflammatory bowel disease.

Applicants respectfully remind the Examiner that M.P.E.P. § 2112 requires the Examiner to provide a rationale or evidence tending to show inherency. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte* Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. § 1990) (Emphasis in original). Thus, for a claim to be rejected on the basis of inherency, the Examiner has the burden to show that a missing element of a claim is inherently present in the prior art and that this missing descriptive matter would be recognized by persons of skill in the art.

Applicants respectfully assert that the prior art does not inherently anticipate the claimed invention. The following provides the legal foundation for this conclusion.

In *In re Zierden*, 162 USPQ 102 (CCPA 1969), the question presented was whether claims to a method of removing alluvium from industrial waters, for example water in cooling systems, were anticipated by a prior art reference [French patent] that disclosed a method for treating industrial waters to remove calcium carbonate scale that builds up in such cooling systems. The court held that because the prior art reference did not inherently teach that the industrial waters contained alluvium, the disclosed method did not necessarily result in the removal of alluvium. Thus, there was no anticipation of the claimed invention.

The dissenting judge stated that "if the industrial waters of the [prior art] French patent contain alluvium, even in a very slight amount, then the process of that patent inherently anticipates appellant's process as claimed here." (Emphasis added) There was no dispute between the majority and the dissent that if alluvium had been present in the waters, the prior art process would have inherently removed the alluvium. (Emphasis added). Further, it was not disputed that it was very likely that alluvium was present in the waters. The court's decision was based on the lack of certainty that alluvium was present in the waters.

In *Hansgirg v. Kemmer*, 102 F.2d 212, 40 USPQ 665 (CCPA 1939), the court emphasized that for a prior art reference to anticipate a claimed invention, the matter not explicitly described in the reference must necessarily be present in the reference. The court held that "[i]nherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient."

The law on probabilistic inherency is set forth in *Continental Can v. Monsanto*, 948 F.2d 1264, 20 USPQ2d 1746 (Fed. Cir. 1991). The court held that "[t]o serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing

described in the reference, and that it would be so recognized by persons of ordinary skill." (Emphasis added).

Claim 7 is amended herein to recite "[a] method of method of treating inflammatory bowel disease in a human subject, comprising administering to a subject an amount of a ligand of complement receptor 3 or complement receptor 4 effective in downregulating production of interleukin-12, thereby treating the inflammatory bowel disease." Thus, for any reference to anticipate under the doctrine of inherency, the reference must establish with certainty that a subject with inflammatory bowel disease was treated in the method described. If amended claim 7 is rejected for allegedly being anticipated on the basis that Rosen et al. inherently describes each element of the claimed invention, the Office has the burden to show that the missing element (treating inflammatory bowel disease in a subject) is inherently described. This inherency must be non-probabilistic, i.e., it must be a matter of certainty that the "missing" element of the claim is in the prior art. *Hansgirg* at 214. In the absence of such evidence, the Office fails to make its *prima facie* case of anticipation, and the rejection must be withdrawn.

Rosen et al. provide an anti-CR3 antibody that inhibits the recruitment of myelomonocytic cells to an inflammatory site *in vivo*. Specfically, Rosen et al. studied the effects of an anti-CR3 antibody on footpad swelling in a mouse model. There is no evidence to show or allow one of skill in the art to recognize that any of the subjects utilized in these studies had inflammatory bowel disease and were treated for

inflammatory bowel disease by the method of Rosen et al. Therefore, it is clear that the population of subjects utilized by Rosen et al. did not necessarily (i.e. with certainty) include a subpopulation of subjects who had inflammatory bowel disease. Thus, a subject with inflammatory bowel disease was not necessarily treated by Rosen et al. If the Office continues to assert the inherency of claim 7 based on Rosen et al., the Office has the burden to show that the missing matter in this reference, treatment of a subject with inflammatory bowel disease, is necessarily present in Rosen et al. *Hansgirg*.

The Examiner has failed to show with certainty that the missing matter is present, and thus there can be no anticipation of claim 7 based on inherency. Therefore, applicants respectfully request that this rejection be withdrawn as it applies to claim 7 and its dependent claims (claims 8 and 10).

B. The Office Action states that claims 1-8 and 10 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Gorden et al. (J. Neuroimmunology 62: 153-160 (1995) (IDS). Also stated in the Office Action is that Gorden et al. teach a method of administering an antibody with specificity for CR3 for treatment of the autoimmune disease EAE, and consequently its symptoms, as recited in the instant claims. Though the referenced teachings do not explicitly teach that administration of antibodies directed to CR3 downregulates interleukin-12 in a subject or treats an interleukin-12 induced inflammatory response, down regulation of interleukin-12 in a subject and treatment of

an interleukin-12-induced inflammatory response would be inherent properties effected by administration of antibodies against CR3. Therefore, according to the Office Action, the referenced teachings anticipate the claimed invention.

As stated above, claim 7 now recites "[a] method of method of treating inflammatory bowel disease in a human subject, comprising administering to a subject an amount of a ligand of complement receptor 3 or complement receptor 4 effective in downregulating production of interleukin-12, thereby treating the inflammatory bowel disease." Thus, for any reference to anticipate under the doctrine of inherency, the reference must establish with certainty that a subject with inflammatory bowel disease was treated in the method described. If amended claim 7 is rejected for allegedly being anticipated on the basis that Gordon et al. inherently describes each element of the claimed invention, the Office has the burden to show that the missing element (treating inflammatory bowel disease in a subject) is inherently described. This inherency must be non-probabilistic, i.e., it must be a matter of certainty that the "missing" element of the claim is in the prior art. *Hansgirg* at 214. In the absence of such evidence, the Office fails to make its *prima facie* case of anticipation, and the rejection must be withdrawn.

As stated by the Examiner, Gordon et al. describe a method of administering an antibody with specificity for CR3 for treatment of the autoimmune disease EAE, and consequently its symptoms. There is no evidence to show or allow one of skill in the art to recognize that any of the subjects utilized in these studies had inflammatory bowel

disease and were treated by the method of Rosen et al. Therefore, it is clear that the population of subjects utilized by Rosen et al. did not necessarily (i.e. with certainty) include a subpopulation of subjects who had inflammatory bowel disease. Thus, a subject with inflammatory bowel disease was not necessarily treated by Rosen et al. If the Office continues to assert the inherency of claim 7, based on Rosen et al., the Office has the burden to show that the missing matter in this reference, treatment of a subject with inflammatory bowel disease, is necessarily present in Rosen et al. *Hansgirg.*

The Examiner has failed to show with certainty that the missing matter is present, and thus there can be no anticipation of claim 7 based on inherency. Therefore, applicants respectfully request that this rejection be withdrawn as it applies to claim 7 and its dependent claims (claims 8 and 10).

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of the application to issue.

A check in the amount of $ 920.00 (extension of time fee) and a Request for Extension of Time are included herewith. This amount is believed to be correct. However, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Alexandria, Virginia, 22313-1450, on the date shown below.

Gwendolyn D. Spratt — Date: 4-1-03

Marked-Up Version of Claim Amendments
Serial No. 09/196,867

7. (Amended) A method of treating [the interleukin-12 induced inflammatory response of an] inflammatory bowel disease in a human subject, comprising administering to a subject an amount of a ligand of complement receptor 3 or complement receptor 4 effective in downregulating production of interleukin-12, thereby treating the interleukin-12 induced inflammatory response of an inflammatory bowel disease [, wherein the ligand is not monoclonal antibody 5C6].

10. (Amended) The method of claim [1, 2, 3, 4, 5, 6,] 7 or 8, wherein the ligand of complement receptor 3 is selected from the group consisting of iC3b, ICAM-1, fibrinogen, β-glucan, C3b, ICAM-2, ICAM-3, a complement receptor 3-binding microorganism, a complement receptor 3-binding product of a complement receptor 3-binding microorganism and antibodies to complement receptor 3 [which are not monoclonal antibody 5C6].